T-1, P-1

FDA TSE Advisory Committee Meeting
January 18, 2001
Topic 1.
Suitability of Blood and Plasma Donors Who Traveled or Lived in BSE Countries: Further Consideration

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US Public Health Service Advisory Committee on Blood Safety and Availability
(Concerns Expressed to PHS Jan 1998)

- There is no demonstrated risk to recipients of CJD-implicated plasma derivatives—theoretical only.
- Processing greatly reduces infectivity in fractions IV, V.
- CJD withdrawals do not substantially reduce theoretical risk. (≥25% of large plasma pools used to produce derivatives are likely to contain contribution from a donor who will ultimately get sporadic CJD.)
- No screening question can defer or pre-morbid laboratory test detect those donors.
- Withdrawals failed to retrieve most CJD-implicated product.
- CJD withdrawals contributed significantly to shortages of some plasma derivatives.

Guidance for Industry:
Revised Precautionary Measures to Reduce Possible Risk of Transmission of CJD & vCJD by Blood & Blood Products
(CBER Sept 98, rev Aug 1999 recommended for immediate implementation)

- Continued deferral of donors with CJD or increased risk of CJD
- Continued quarantine of blood and components (including plasma) from donors with CJD or increased risk of CJD
- **No withdrawal of plasma derivatives prepared from pools to which donors with classical CJD or increased risk of classical CJD contributed**
- **Withdrawal of plasma derivatives and quarantine of intermediates prepared from pools to which any donor who develops new-variant CJD contributed (has not occurred)**

(Risk factors for CJD=PRNP mutation associated with fCJD or GSS, recipient of dura graft or of human pituitary hormone.)
[Full document available at www.fda.gov/cber/guidelines.htm])

Reasons for Increased Concern about Blood Donors During Incubation Period of vCJD

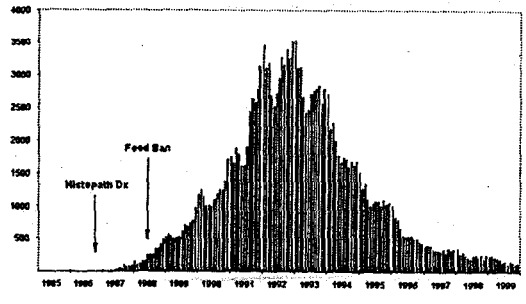
- vCJD is an emerging infection not found in USA.
- Less is known about pathogenesis of vCJD than sporadic CJD (sCJD).
- Lymphoid tissues in vCJD contain detectable protease-resistant prion protein while in sCJD do not.
  Infectivity of those tissues is not yet clear. (Note: Lymphoid tissues of some patients with conventional forms of CJD have been infectious [Brown P et al. Ann Neurol 1994;35:513].) Implication: Blood, which contains lymphoid cells, might be more infectious in vCJD than in other forms of CJD.
- In 1998, UK authorities decided not to source plasma for fractionation from UK donors (which implies lack of confidence).

FDA Guidance for Industry:
Revised Precautionary Measures to Reduce Possible Risk of Transmission of CJD & vCJD by Blood & Blood Products (cont.):
Response to TSEAC Advice of 18 Dec 1998, 2 June 1999
(CBER Aug 1999, revised Nov 1999, recommended for implementation by Apr 17, 2000)

- **Deferral of donors who resided in UK for ≥6 mo (cumulative) between 1 Jan 1980 and 31 Dec 1996**
- **Deferral of donors who received injected UK bovine insulin**
- Retrieval of blood and blood components (including plasma) from donors deferred because of UK residence or exposure to injected UK bovine insulin
- **No withdrawal of plasma derivatives for UK residence or exposure to injectable bovine products from BSE countries**
- Commitment to monitor effect of revised blood policy on blood supply and reevaluate policy frequently

(UK=England, Northern Ireland, Scotland, Wales, Isle of Man, Channel Islands)

Cases of BSE Registered in Great Britain through 1999 (MAFF)



USDA (APHIS) Interim Regulation Regarding BSE and European Ruminant Products

- Dec 1997 (FR Jan 6, 1998): Pending clarification of the status of European countries, as a preventive step, the USDA prohibited importation of all live ruminants and most ruminant products (excluding gelatin [for human consumption], milk and milk products) from all countries of Europe due to potential risk of BSE.

Recent Concerns about BSE and vCJD Outside UK

- Recognized that substantial exports of UK cattle, beef and beef products as well as meat-and-bone meal to several European countries continued during high-BSE years.
- Rates of new diagnoses and deaths from vCJD increased in UK.
- Diagnosed BSE cases have increased in several European countries and new countries have recognized disease.

Other Information Recent Concerns about BSE and vCJD

- Preliminary report of TSE transmitted by transfusion of blood drawn during the asymptomatic incubation period of a sheep experimentally infected with the BSE agent to healthy sheep obtained from a TSE-free source.
- Health Canada issued a precautionary directive for deferral of blood and plasma donors who spent extended periods of time in France.
- US Department of Defense recognized that some US military personnel and dependents in Europe consumed beef products obtained from the UK.

Suitability of Blood and Plasma Donors Potentially Exposed to BSE Agent: Program

1. Recent events concerning vCJD and BSE in the UK, France, and other European countries
2. Health Canada assessment of risk and policies for deferral of blood donors who spent time in France
3. Potential dietary exposures of US military personnel and families in Europe to BSE agent
4. Possible effects of FDA deferral policies on the US blood supply

Suitability of Blood and Plasma Donors Potentially Exposed to BSE Agent

CHARGE

Please evaluate new information concerning vCJD in the UK and France and BSE in the UK, France and other European countries where the disease has infected or may have infected cattle. Address the risk that donors resident in various countries (including overseas US military personnel and dependents) might have been exposed to and infected with the BSE agent and consider implications for the safety of the blood supply.

Suitability of Blood and Plasma Donors Potentially Exposed to BSE Agent

CHARGE (continued)

In the context of a risk-benefit estimate, please consider effects that FDA blood-donor policies may have had on the blood supply in the US as well as effects to be expected if additional deferrals of blood donors are recommended.

TSEAC 18 January 2001
Issue 1. Suitability of Blood and Plasma Donors Potentially Exposed to BSE Agent:
Questions

1. United Kingdom

a. Are recent data on rates of vCJD in the UK or the potential risk of transmitting vCJD by human blood or plasma sufficient to warrant a change in current FDA policies regarding deferrals of blood and plasma donors based on a history of travel or residence in the UK? Please comment.

b. Have recommendations of FDA concerning donor deferral for residence in UK had an adverse effect on the blood supply sufficient to consider a change? Please comment.

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Issue 1. Suitability of Blood and Plasma Donors Potentially Exposed to BSE Agent:
Questions (continued)

2. France

a. Should the FDA recommend deferral of blood or plasma donations by persons with a history of travel or residence in France for an aggregate period of ten years or more after 1980?

b. If not, which years and aggregate duration of residence, if any, should be of concern?

TSEAC 18 January 2001
Issue 1. Suitability of Blood and Plasma Donors Potentially Exposed to BSE Agent:
Questions (continued)

3. Other BSE countries

a. Should the FDA recommend deferral of blood or plasma donations by persons with a history of travel or residence in other countries identified by the USDA as having BSE in cattle for an aggregate period of ten years or more after 1980?

b. If not, which years and aggregate duration of residence, if any, should be of concern?

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Issue 1. Suitability of Blood and Plasma Donors Potentially Exposed to BSE Agent:
Questions (continued)

4. Donors potentially exposed in more than one BSE country

a. Should the FDA recommend deferral of blood or plasma donations based on a donor's history of travel or residence in more than one country identified by the USDA as having BSE in cattle for some combined aggregate period of time?

b. If so, which years and aggregate duration of residence should be of concern?

TSEAC January 18, 2001
Issue 1. Suitability of Blood and Plasma Donors Potentially Exposed to BSE Agent:
Questions (continued)

5. US military personnel and dependents potentially exposed to the BSE agent

Should the FDA recommend deferral of blood or plasma donations based on a donor's history of potential exposure to beef or beef products from the UK while serving in the US military or as a military dependent?